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HEAD AND NECK ONCOLOGY

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Solitary fibrous tumor of the orbit – two cases and a review of the literature

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Abstract Solitary fibrous tumors of the orbit (SFT) are mesenchymal lesions that can develop either as malignant or benign neoplasias. We describe the histological features leading to the diagnosis in two females and review the current literature. Diagnosis of SFT only can be performed by histological examination, since clinical signs and radiological features are not specific enough. Even a malignant or benign course cannot be predicted, since clinical and radiological features do not correlate with histological signs of malignancy and vice versa. Radical resection is the treatment of choice, since no other treatment option has been proven to be efficient.

Keywords Solitary fibrous tumor · Orbit · Immunohistochemistry · Diagnosis · Treatment

Introduction

Orbital tumors can be segregated into vascular, hematopoietic, neural, mesenchymal and inflammatory-induced tumors. In addition, there are neoplasms and cysts from the lacrimal gland, infiltrating tumors from adjacent structures as well as metastases (Table 1). Solitary fibrous tumors (SFT) are rare mesenchymal spindel cell tumors usually occurring in the pleura, but also in many other extra-thoracal areas [26]. Since the first description of orbital SFT by Dorfmann et al. [13] in 1994, the segregation of mesenchymal tumors of the orbit has been enlarged. To our knowledge, there are up to 50 SFTs of the orbit described [1, 4, 5, 6, 8, 13, 15, 16, 17, 18, 19, 20, 21, 26, 27, 28, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46]. The aim of the present study is to present two cases and to review the current literature.

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Subjects and methods

There were two patients with histologically confirmed SFT of the orbit seen in the University Hospital of Zurich between October 2002 and January 2003. Both wee diagnosed, operated on and followed up at the Department of Otorhinolaryngology Head and Neck Surgery, and clinical information was obtained from the files of the University Hospital, Zurich, Switzerland, and follow-up information by contacting the attending physicians. Searching the current literature in the PubMed database, only English and German articles were considered using the keywords "solitary fibrous tumor" and "orbit."

For histological examinations, the specimens were fixed in formalin and embedded in paraffin according to standard procedures. Sections (1–2 mu) were cut for conventional histology and immunohistochemistry. Immunohistochemistry was performed on deparaffinized, pretreated sections (either enzymatical predigestion or heating in citrate buffer for 3 min using a pressure cooker) using the Ventana NexES automated staining system with DAB as substrate. Reactions with antibodies against cytokeratin (Biomedicals AG, Switzerland; dilution 1:250), S100 (DAKO, Glostrup, Denmark; 1:500), CD34 (Serotec, Oxford, UK; 1:20), bcl2 (Dako, Glostrup, Denmark; 1:200) and CD99 (Novocastra Laboratories, Newcastle upon Tyne, UK; 1:25) were performed. The quality of the reactions was controlled on tissue slides with known reaction patterns stained in parallel with the examined probes.

Case 1

Eighteen years prior to this presentation, this 77-year-old female had undergone an angiography and superselective embolization for an extraconal suspected hemangioma in the left orbit and remained blind as a consequence of this procedure. Seven years ago (1995), the tumor had to be excised surgically because of progressive growth using a superotemporal orbitotomy (i.e., Krönlein procedure). During the surgery, the tumor was well circumscribed and separated from adjacent tissue by a capsule-like structure. Except for the amaurosis on this side, she remained symptom free until 12 months prior to referral with a progressive swelling of the lateral aspect of the left lower eyelid and a mild painless proptosis.

Table 1 Differential diagnosis of orbital tumors [2, 41]

Vascular	Hematopoietic	Neural	Mesenchymal	Inflammatory	Varia
Cavernous hemangioma	Lymphoid	Schwannoma	Rhabdomyosarcoma	Endocrine orbitopathy	Lacrimal gland tumor
Capillary hemangioma	Leukemia	Optic nerve glioma	Leiomyoma	Orbital pseudotumor	Mucocele
Lymphangioma	Langerhans' cell histiocytosis	Orbital meningioma	Leiomyosarcoma	Cellulitis/abscess	Dermoid
			Lipoma		Infiltrating tumors from adjacent structures
			Liposarcoma		Metastasis
			Fibrous dysplasia		
			Osteoma		
			Osteosarcoma		
			Fibroma		
			Fibrous histiocytoma		
			Fibrosarcoma		
			Fibromatosis		
			Nodular fasciitis		
			Solitary fibrous tumor		

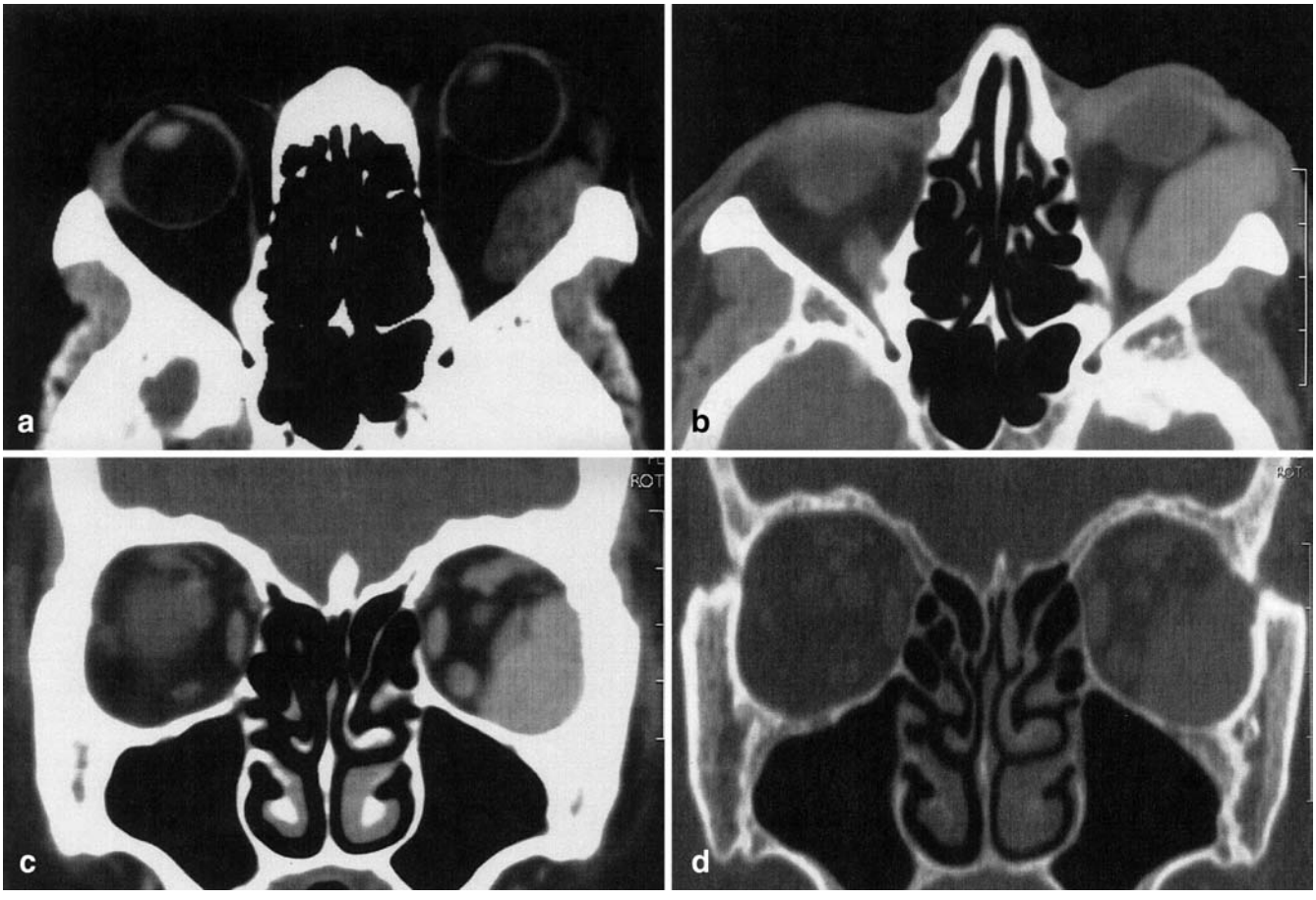

Fig. 1 Solitary fibrous tumor of infero-lateral quadrant of left orbit. The axial noncontrast CT depicts a well-defined ovoid-shaped lesion, isodense compared to muscle (**a**) with marked homogeneous contrast enhancement (**b**). The globe is displaced anteriorly. The coronal images (**c**, **d**) show the lateral rectus muscle medially displaced corresponding to an "extraconal" origin of the tumor that lacks osseous changes on HR bone window images (**d**)

The noncontrast and contrast-enhanced computed tomography examination of the orbit showed an extraconal 3×1.5×2.5-cm tumor in the lateral aspect of the left orbit. The lateral rectus muscle was not infiltrated, but displaced medially. There were no calcifications within the lesion, showing a homogeneous contrast uptake (Fig. 1a–d). Magnetic resonance imaging (MRI) was not performed. Radical excision by a coronal incision, including releasing the temporal mus-

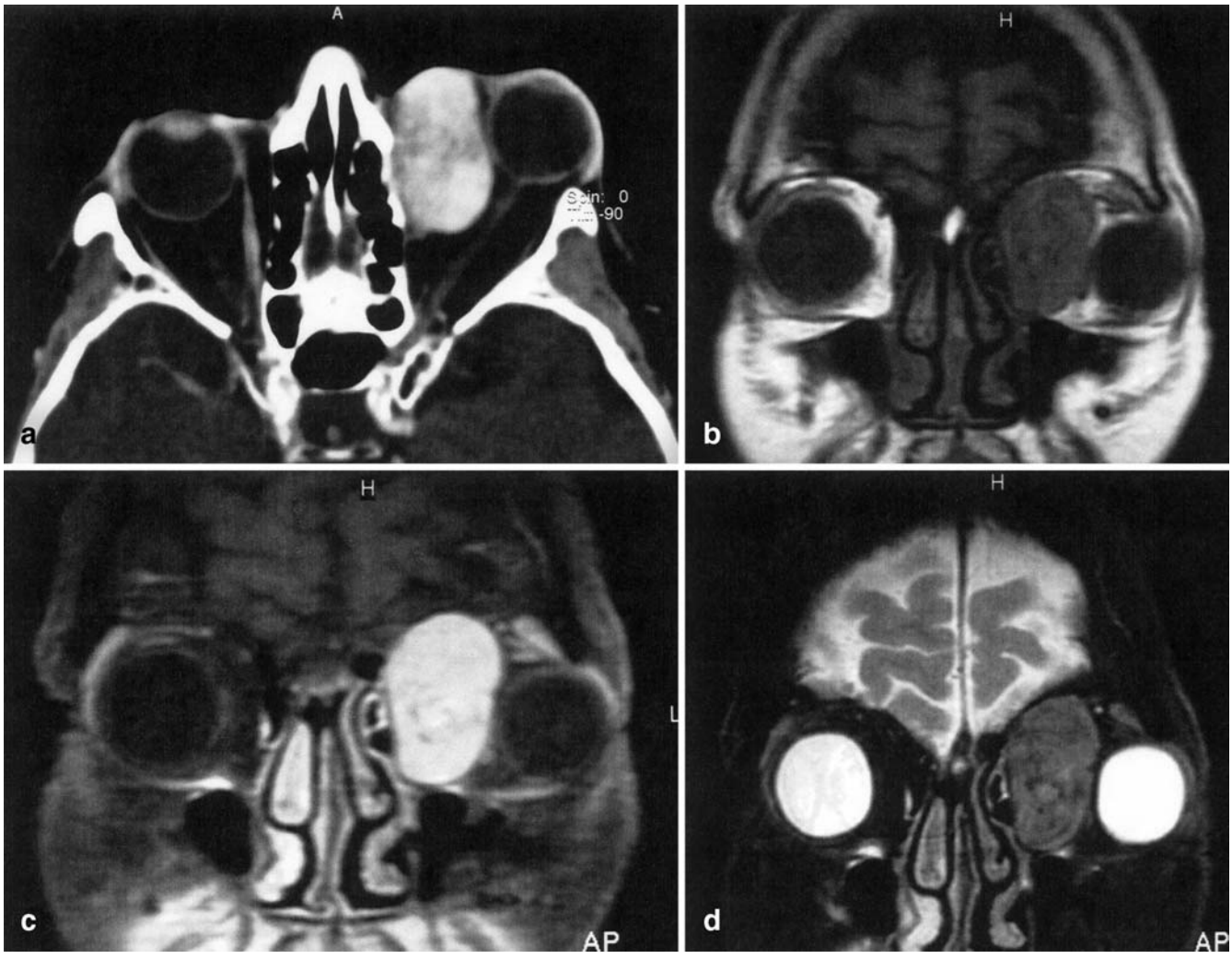

Fig. 2 Solitary fibrous tumor of left medial orbit. A markedly enhancing well-defined ovoid lesion is visible stretching the optic nerve because of displacement of the globe antero-laterally (**a**). The left orbit appears slightly enlarged because of flattening and thickening of the medial orbital wall. The extraconal tumor location is delineated to better advantage on the coronal T1-weighted noncontrast MR image (**b**). Following contrast administration (**c**) the tumor shows marked signal intensity increase. On the T2-weighted coronal image (**d**), a hypointense (*dark*) signal is present reflecting the fibrous and cellular nature of the lesion

cle and temporarily removing the lateral wall of the orbit, was performed. The patient died of cardiac problems 6 months after the last operation.

Case 2

This 75-year-old female had noticed a slowly progressing swelling in the medial canthus on the left side for 2.5 years. This swelling was not painful and caused no double vision, but induced intermittent epiphora. On clinical examination, there was a marked displacement of the globe inferiorly and laterally, and in the medial canthus area, there was a well-divided tumor with a smooth surface. There was no hypaesthesia.

On contrast-enhanced MRI, there was a 2×2×3-cm extraconal and well-defined tumor, which was homogeneous, situated adjacent to the medial orbital wall and slightly flattened. On T1, the tumor was isointense relative to gray matter and after contrast homogeneously hyperintense with hypointense foci (Fig. 2a–d), while on CT the tumor showed mild pressure erosion of the lamina papyracea. A fine-needle biopsy was performed. The tumor could be removed radically by a Linch incision. The tumor was of white color and was well divided from the adjacent structures (medial rectus muscle). The patient recovered without sequelae and has been symptom free up to 7 months.

Results

Pathology

Case 1

The 1995, the resected tumor measured 2.7×1.4×0.6 cm. Histology showed focally strongly collagenized tissue consisting of bland spindle cells with alternating cellularity and patternless architecture. Many fine branching blood vessels were seen, leading initially to the false interpretation of the tumor as a hemangioma. The mitotic activity was low (less than one mitotic figure per ten high power fields). The resection margins were involved. The recurrent tumor was resected in 2002 in two parts measuring

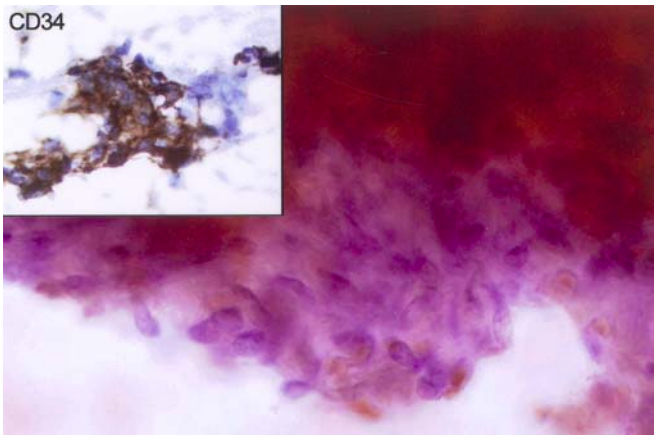

Fig. 3 Fine-needle aspirate (Papanicolau staining) showing spindle mesenchymal cells without any significant pleomorphism. The immunocytochemical reaction with an antibody against CD34 is shown in the *upper left* with brown reaction product

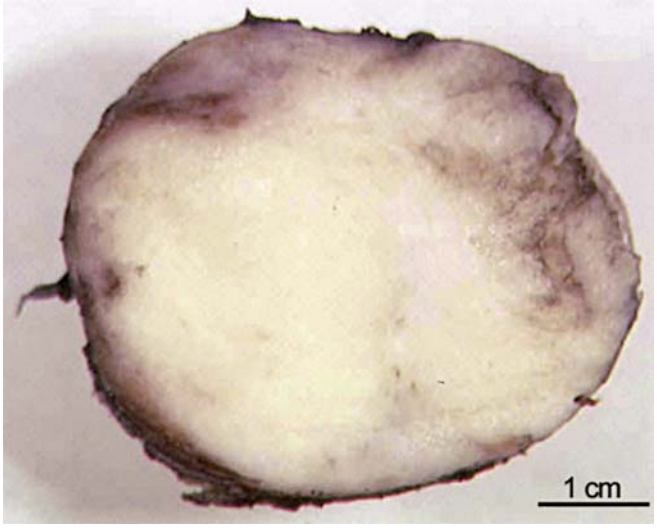

Fig. 4 Cut surface of the solitary fibrous tumor of the second patient

1.2 and 2.5 cm. The solid, firm cut surface was gray to slightly tan. Compared to the tumor resected in 1995, the cellularity, atypia and mitotic rate (four to five mitotic figures per ten high power fields) were increased. No necrosis or infiltrative growth was seen. Positivity for CD 34 and bcl2 was demonstrated in both of the tumors resected in 1995 and 2002. During the autopsy 6 months after the last operation, no recurrent tumor or metastases were demonstrated.

Case 2

The fine-needle aspirate contained few cohesive groups of monomorphic spindle cells with sparse cytoplasm (Fig. 3). Immunocytochemically, a distinct positivity for CD 34 could be demonstrated (Fig. 3, upper left). The preferred diagnosis was solitary fibrous tumor. The resected

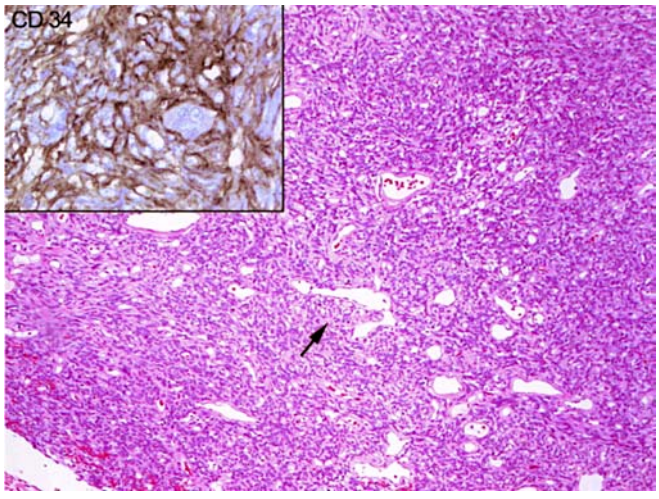

Fig. 5 Histology (standard hematoxilin and eosin staining) of the tumor of the second patient with an *arrow* pointing to a typical branching "hemangiopericytoma-like" blood vessel. Bland spindle cells in patternless arrangement with strong positive reaction for CD 34 (*upper left*)

tumor (Fig. 4) was firm, well circumscribed and measured 3.2×2.9×2.0 cm, with a solid, whitish cut section. A microscopically moderately cellular tumor with alternating hypocellular and more cellular areas was found (Fig. 5). Thick collagen fibers, perivascular fibrosis and a rich network of branching blood vessels could be seen. The mitoses were rarely seen, not exceeding three normal mitotic figures per ten high power fields. No necrosis or atypia was demonstrated. Immunohistochemically strong diffuse positivity for CD 34 (Fig. 5, upper left) and a focally positive reaction for bcl2 and CD99 were found, all other markers being negative.

Review of the current literature

According to the present literature, 50 patients have been described with orbital SFT (Table 2). In 9 out of 50, the histological work-up is not described, and in 20, no follow-up is indicated. For 25, it occurred on the left side and for 14 on the right orbit, and for 11, the affected side was not indicated. The most often described tumor locations were extraconally in 11 cases (22%) and intraconally in 3 cases (6%), either in the superomedial quadrant (11 cases, 22%) or adjacent to the lacrimal gland (6 cases, 12%). From the first clinical manifestation to diagnosis, there was a mean course of 24.6 months. The mean age for all 50 patients was 43.2 years (from 14 to 76 years), while the male to female ratio was 28:22. The most frequent findings were progressive painless proptosis (n=29, 58%), epiphora (n=6, 12%) and a clinically detectable mass within the orbit.

Twenty-four out of the 50 (48%) described tumors were described clinically as benign, while 15 (30%) showed an aggressive course with local recurrences (n=6; 12%), invasive growth (n=6; 12%) or both (n=2, 4%). Distant metastasis after 7 years was described in one [26]. In 11 (22%)

Table 2 Review of the literature. *Rec* recurrence, *B* benign; *a1* one histologic sign of malignancy, *NR* not reported

Patient number	Reference	Age (years)/ sex	Clinical presentation	Course	Histology	Follow-up (months)	Localization in orbit
1	[1]	66/f	Proptosis, tearing, foreign body sensation	Aggressive (invasive)	B	NR	Floor of orbit, medial, intra-and extraconal
2	[3]	67/m	Proptosis, tearing	B	NR	44	Lacrimal grand fossa
3		14/f	Proptosis, tearing, blurred vision	Aggressive (rec)	NR	37	Superomedial, anterior
4		37/m	Proptosis, headache	B	NR	24	Superomedial, anterior
5	[4]	18/m	Painless proptosis	B	a1	7	Superomedial
6	[5]	50/m	Swelling	Aggressive (invasive)	b	48	Upper half
7		24/m	Swelling, proptosis	Aggressive (rec)	b	60	Lacrimal gland region
8		70/m	Proptosis	Aggressiv (rec)	a1	36	Retrobulbar
9	[6]	54/m	Proptosis, downward displacement of the eye	B	B	9	Retro-und suprabulbar
10	[1]	54/m	Proptosis, double vision, swelling	Aggressive (rec)	a1	NR	Extraconal inferolateral, extradural middle cranial fossa, cavernous sinus
11	[9]	4O/f	Swelling, proptosis, dislocation of eye	Aggressive (invasive)	B	NR	Superolateral
12	[10]	15/m	Painless proptosis, eye displacement	Aggressive (invasive)	B	12	Superolateral apex, extraconal
13	[11]	69/m	Diplopia	Aggressive (rec, invasive, dead of disease)	NR	240	NR
14	[12]	38/f	Proptosis	B	B	15	Superomedial
15	[14]	25/m	Gradual proptosis, painless rubbery mass	B	a1	24	Superolateral in lacrimal fossa
16	[15]	64/m	Proptosis	Aggressive (rec, invasive dedifferentiation)	a1	96	Superior, extraconal
17	[16]	14/f	Painless proptosis, upper lid swelling	Aggressive (rec)	NR	NR	Superomedial, anterior, extraconal
18	[20]	35/f	Pressure	B	B	12	Medial, extraconal
19	[21]	58/m	Proptosis, headache	B	B	NR	Lateral, extraconal
20	[24]	24/m	Swelling upper lid, limited mobility upgaze	B	B	27	Lacrimal gland region, extraconal
21		26/f	Upper lid swelling, diplopia upward	B	B	11	Lacrimal gland region
22		40/f	Progressive, painless proprosis	B	B	28	Retrobulbar
23	[29]	61/m	Slowly progressive, painless proptosis	Aggressive (invasive)	NR	NR	Lateral, intraconal
24	[31]	62/m	Slowly progressive, painless proptosis	Aggressive (invasive)	B	12	NR
25	[33]	21/m	NR	B	B	24	NR
26	[34]	48/f	Proptosis, worsening vision, limited extraocular movement	NR	NR	NR	Superomedial, retroorbital
27	[35]	43/f	Slowly progressive, painless proptosis	B	B	NR	Superolateral, extracoronal
28	[36]	75/m	Slowly progressive, painless proptosis	B	B	1	Superior, retrobulbar
29	[31]	231m	Slowly progressive, painless proptosis	B	NR	9	Superomedial
30	[38]	23/f	Watery left eye, painless swelling medial canthus, rabbery mass	NR	B	NR	Medial anterior
31	[39]	21/m	Proptosis	B	B	22	Medial
32	[41]	60/m	NR	NR	B	NR	NR

Table 2 (continued)

Patient number	Reference	Age (years)/ sex	Clinical presentation	Course	Histology	Follow-up (months)	Localization in orbit
33		63/f	NR	NR	B	NR	NR
34	[42]	44/m	Slowly progressive, painless proptosis	B	B	18	Medial
35		65/f	Slowly progressive, painless proptosis	B	B	144	Medial
36		69/f	Slowly progressive, painless proptosis	Aggressive (rec)	a1	NR	NR
37	[46]	76/m	Ptosis, pressure	B	B	12	Superolateral in lacrimal fossa
38	[47]	24/f	Blurred vision	NR	B	NR	Superomedial
39		69/m	Proptosis	NR	B	NR	Superomedial
40		72/m	None	NR	B	NR	Inferolateral
41		45/f	Eyelid swelling	NR	B	NR	Superolateral
42		31/m	Proptosis	NR	B	NR	Superolateral
43		18/f	Ptosis, palpable mass	NR	B	NR	Inferior
44	[48]	40/f	Tearing, disturbed vision, swelling left upper lid, mass	B	B	18	Superolateral, extraconal
45		20/f	Watery eye, swelling	B	B	23	Anteromedial floor of orbit
46		19/f	Swelling, mass	B	B	72	Lower anterior orbit into lower eyelid, extraconal
47		32/f	Slowly progressive, painless proptosis	B	B	NR	Lateral intraconal
48		48/m	Slowly progressive, painless proptosis	NR	NR	NR	Superomedial
49		48/f	Upper eyelid swelling	Aggressive (metastasis)	B	94	Upper eyelid
50		39/m	Proptosis	B	B	5	NR

cases, the clinical course was not indicated. However, only 4 (27%) of the 15 clinically aggressive growths had histological signs of malignancy, whereas 7 (47%) showed no such signs, and in four no grading was indicated. Among the 24 clinically benign lesions, histology was benign in 19 (79%), malignant in 2 (8%), and in the remaining three, no histological investigation was indicated. In summary, in more than 30% of the orbital SFT, a clinically aggressive course can be expected.

Discussion

In contrast to the first description in 1931 by Klemperer und Rabin [26], ultrastructural, immunohistochemical as well as electron microscopic investigations of SFT revealed that this tumor has to be considered as having a mesenchymal, submesothelial origin [10, 46]. Most SFTs are seen in the pleura and less frequently in the Jung, mediastinum, pericard, dura, upper respiratory tract, salivary gland, thyroid gland, peritoneum, liver, retroperitoneal space, pelvis, adrenal gland, kidney, bladder, prostate gland, cervix, spinal cord, periosteum and soft tissue [26]. According to the ENT literature, there are case reports involving the upper respiratory tract, i.e., the nasal cavity, the paranasal sinuses as well as in the epipharynx [47, 48]. These described tumors did not show an aggressive clinical course and were not revealed to be malignant at histological examination [47, 48]. Twelve to 23% of pleural SFT show an aggressive clinical course with infiltration into adjacent structures, recurrences and/or metastases [3, 14]. Although worrisome histological features of malignancy (i.e., hypercellularity, cytologic atypia, tumor necrosis and increased mitotic rate with more than four mitoses per ten high power fields) were described, there is no strict correlation between morphology and behavior.

Radical surgical resection seems to be the most important prognostic factor according to a study on 223 pleural SFT in which 82 (36.8%) were histologically malignant. Forty-five percent of the latter could be healed successfully by resection alone. Most of them were pedicled or circumscribed [3, 14]. However, there were lesions with aggressive courses despite lacking signs of malignancy on histology, as in our case 1 [3]. The high incidence of extrapleural manifestations contradicts the hypothesis of a mesothelial origin of SFT.

To our knowledge, 50 orbital SFT have been described, apart from our two cases (Table 2). The clinical picture of our two cases is very similar to most of the described cases. Neither clinical presentation nor the localization of SFT within the orbit is specific [32]. SFT can occur at any age (mean age 43.2 years), even in children [1, 32, 36].

Our cases demonstrated histologically the typical morphology of the solitary fibrous tumor: well-circumscribed, firm, solid tumors consisting of rather bland spindle cells haphazardly arranged in alternating hypo- and hypercellular areas with intervening thick collagen fibers. Patternless architecture without a tendency to form bundles as well as perivascular fibrosis are characterictic. A rich network of typically branching, staghorn, so called "hemangiopericytic" blood vessels are at least focally prominent. Neither morphologic nor immunohistochemical features of epithelial, neural or myogenic differentiation are observed. Sometimes myxoid areas or a few adipocytes can be found. The worrisome histological signs have been discussed above and must be sought after in representatively sampled tumor tissue by the pathologist. In a typical case of a solitary fibrous tumor, the histological diagnosis is fairly easy if considered. Small biopsies may make the diagnosis difficult, especially if the clinical context is not known to the pathologist. The immunohistochemical profile (positivity for CD34, bcl2 and often CD99) is helpful, although non-specific without the proper morphologic correlation. CD 34 (human hematopoietic progenitor cell antigen), which is consistently expressed in solitary fibrous tumor, is also expressed in a broad range of various soft tissue mesenchymal tumors (dermatofibrosarcoma protuberans, neural tumors, epithelioid sarcoma and Kaposi sarcoma). Similarily, bcl2 and CD99 can be found in various other mesenchymal lesions. No typical genetic alterations in SFTs have been identified to date [25]. Solitary fibrous tumor is thought to be of a fibroblastic nature. The diagnosis of a solitary fibrous tumors can be suspected already cytologically on fine-needle aspiration [6], as shown in our case 2.

The histological differential diagnosis of the solitary fibrous tumor is primarily hemangiopericytoma, which is at present histopathologically a very disputed entity. It seems that this entity, first described in the 1940s by Stout [25], is composed of many very different entities, which have one thing in common: "hemangiopericytic"-like, branching blood vessels. The new classifications separate these pooled tumor types into synovial sarcomas, mesenchymal chondrosarcomas, solitary fibrous tumor and others. There is still a subset of tumors, which morphologically can be diagnosed as hemangiopericytoma (and is strongly positive for CD 34), but – interestingly – its prognostic features seem to be very similar to SFTs. Giant cell angiofibroma, first described in 1995 [9] and often occurring in the orbita, is nowadays considered as a morphologic variant of the solitary fibrous tumors containing multinucleated stromal giant cells and angectoid spaces [24]. Other tumors that have to be considered are benign and malignant neural tumors, meningeoma as well as benign deep fibrous histiocytoma.

On CT, this lesion shows a heterogeneous pattern in the contrast-enhanced sequences and is sharply defined [20]. Hypodense areas within the tumor may represent myxoid structures. MR imaging of orbital SFT are far more characteristic. In the T1 sequences, they are isointense to gray matter with moderate homogeneous or heterogeneous gadolinium enhancement, while on T2 they are hypointense. SFTs frequently show centrally located, strongly hypodense foci in T1 as well as in T2, representing collagen-rich areas [7, 20]. Other collagen-containing tumors such as fibromatosis, sclerotic pseudotumors or scirrhous carcinoma metastases show a similar T1 and T2 pattern. However, the latter are not as sharply separated from the adjacent tissue. Contrary to SFT, cavernous hemangiomas predominantly occur within the muscle cone and exhibit a high signal on T2-weighted sequences. The role of fluorodeoxyglucose positron emission tomography (PET) has not yet been defined [28].

The aggressive SFT form of the orbit with its invasive growth, local recurrence or metastasis seems to occur more frequently (i.e., 30%) than in pleural SFT [3, 14, 26]. Several studies point to the fact that no conclusion of the clinical course can be drawn from the histological findings [39]. There are histologically malignant tumors having both an aggressive as well as benign outcome; on the other hand, histologically benign features are no guarantee of a good outcome. Hence, Iong-term fellow-up is mandatory.

Radical resection not only provides a good specimen for diagnostic analysis, but also seems to be proven to be the therapy of choice, since radiotherapy as well as chemotherapy are not proven to be effective [6,12, 40]. In addition, radical surgery is even more advantageous for a good prognosis than histological signs of malignancy [3, 5, 20]. However, only in two out of the eight local recurrences described in the literature were the primary resections described as not having been performed radically [1, 28].

Conclusion

Whenever a mesenchymal tumor of the orbit is suggested, SFT should be listed in the differential diagnosis. Thirty percent show an aggressive course with local invasive growth, local recurrence or metastasis. Histological signs do not correlate with clinical behavior. Diagnosis only can be made providing there is evidence of histological features, immunohistological evidence of diffuse CD-34 and vimentin positivity. There are no specific features of radiological imaging showing moderate homogeneous or heterogeneous contrast enhancement. Complete resection is the therapy of choice, although the effect of radiotherapy has not been evaluated. Radical resection seems to be more important for prognosis than histological evidence of malignancy.

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